Rev Bras Anestesiol. 2016;xxx(xx):xxx–xxx

View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector

Sociedade Brasileira de Anestesiologia
REVISTA BRASILEIRA DE ANESTESIOLOGIA
Publicação Oficial da Sociedade Brasileira de Anestesiologia
www.sba.com.br

SCIENTIFIC ARTICLE

Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study

Kentaro Ouchi*, **Kazuna Sugiyama**

Department of Dental Anesthesiology, Field of Oral and Maxillofacial Rehabilitation, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

Received 25 November 2015; accepted 16 December 2015

KEYWORDS
Remifentanil;
Urine output;
General anesthesia

Abstract
Background: An increase in urine output by remifentanil injection during laparoscopic procedures and surgeries such as cardiac and gynecological procedures, due to suppression of the stress response to surgery, has been reported. The aim of our prospective, observational, cohort study was to assess the effect of remifentanil analgesia on urine output during dental and minor oral surgery by comparing intraoperative urine output under defined infusion volumes with and without the use of remifentanil.
Methods: Dental patients aged 16 years or older, American Society of Anesthesiologists physical status 1, with no renal diseases or abnormal blood values of serum creatinine and BUN, not on treatment with diuretic drugs, and undergoing minor oro-maxillofacial surgery or dental treatment under inhalation general anesthesia were included in this study. Urethral catheterization was performed after anesthesia induction, and urine output was measured every 30 min. We measured urine volume (mL) and rate of urine output (mL/kg/h) intraoperatively, and compared these parameters between patients who did and did not receive remifentanil during the intraoperative period.
Results: Eighty-seven patients were categorized into the remifentanil group ($n = 43$) or remifentanil non-use group ($n = 44$). Both volume of urine (mL) and rate of urine output (mL/kg/h) were not significantly different between the two groups (remifentanil group, 372.3 ± 273.5 mL, 1.8 ± 1.1 mL/kg/h; remifentanil non-use group, 343.3 ± 283.3 mL, 1.9 ± 1.2 mL/kg/h; $p = 0.63$; 0.57).

* Corresponding author at: Department of Dental Anesthesiology, Field of Maxillofacial Diagnostic and Surgical Sciences, Faculty of Dental Science, Kyushu University Graduate School, Fukuoka, Japan.
E-mail: ken2006anes@yahoo.co.jp (K. Ouchi).

http://dx.doi.org/10.1016/j.bjane.2015.12.004
0104-0014/© 2016 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Please cite this article in press as: Ouchi K, Sugiyama K. Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study. Rev Bras Anestesiol. 2016. http://dx.doi.org/10.1016/j.bjane.2015.12.004

Conclusion: Our results show that use of remifentanil during dental and minor oral surgeries does not increase urine output.
© 2016 Sociedade Brasileira de Anestesiologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

PALAVRAS-CHAVE
Remifentanil;
Produção de urina;
Anestesia geral

Remifentanil não aumenta a produção de urina durante cirurgia oral, contrariamente ao seu efeito durante outras cirurgias – estudo de coorte

Resumo
Justificativa: Um aumento na produção de urina após a injeção de remifentanil durante procedimentos laparoscópicos e cirurgias cardíacas e ginecológicas, devido à supressão da resposta ao estresse da cirurgia, foi relatado. O objetivo de nosso estudo prospectivo, observacional e de coorte foi avaliar o efeito da analgesia com remifentanil sobre a produção de urina durante cirurgia odontológica e oral de pequeno porte, comparando a produção de urina no intraoperatório sob infusão de volumes definidos, com e sem o uso de remifentanil.
Métodos: Pacientes odontológicos com idades $\geq$ 16 anos, estado físico ASA I, sem doenças renais ou valores sanguíneos anormais de creatinina sérica e uréia, sem tratamento com diuréticos e submetidos à cirurgia bucomaxilofacial de pequeno porte ou tratamento odontológico sob anestesia geral inalatória foram incluídos neste estudo. Cateterismo uretral foi realizado após a indução da anestesia, e a produção de urina foi medida a cada 30 min. Medimos o volume de urina (mL) e a taxa de produção de urina (mL/kg/h) no intra-operatório e comparamos esses parâmetros entre os pacientes que receberam e que não-receberam remifentanil durante o período intraoperatório.
Resultados: Oitenta e sete pacientes foram designados para os grupos com remifentanil (n = 43) ou grupo sem remifentanil (n = 44). O volume de urina (mL) e a taxa de produção de urina (mL/kg/h) não foram significativamente diferentes entre os dois grupos (grupo com remifentanil: 372,3 $\pm$ 273,5 mL, 1,8 $\pm$ 1,1 mL/k/h; grupo sem remifentanil: 343,3 $\pm$ 283,3 mL, 1,9 $\pm$ 1,2 mL/kg/h; p = 0,63; 0,57).
Conclusão: Nossos resultados mostram que o uso de remifentanil durante as cirurgias odontológicas e de pequeno porte não aumenta a produção de urina.
© 2016 Sociedade Brasileira de Anestesiologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob a licença de CC BY-NC-ND (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Reportedly, remifentanil increases urine output during surgery, probably by preventing the stress response to surgery.[1–5] Previous studies on increases in urine output due to remifentanil were performed during laparoscopic, cardiac, or gynecological surgeries, but its effect during oral and maxillofacial treatment has not been reported.

The aim of our observational study was to compare urine output during use of remifentanil versus non-use of remifentanil in patients undergoing minor oral surgery or dental procedures, by measuring urine output under defined infusion volumes in the intraoperative period.

Methods

Dental patients aged 16 years or older, undergoing minor oro-maxillofacial surgery and dental treatment under inhalational general anesthesia at the Clinical Department of Dental Anesthesia, Kagoshima University Medical Dental Hospital from April 2011 to March 2014 were studied. To be included in the study, patients had to be American Society of Anesthesiologists physical status 1. Patients with known renal disease, laboratory data indicative of abnormal blood values of serum creatinine and Blood Urea Nitrogen (BUN), and those on treatment with diuretic drugs were excluded. Informed consent for oral surgery and for participation in this study under general anesthesia was obtained from each patient. The institutional review board of Kagoshima University Medical Dental Hospital approved the study protocol, which was conducted in accordance with the Declaration of Helsinki.

The necessary number of patients required for the study was determined from past and pilot studies, which indicated that at least 41 patients were required in each group to achieve an approximately 27% increase in urine output with remifentanil, at an α risk of 0.05 and $(1-\beta)$ of 0.95.[3] Use of remifentanil was at the attending anesthesiologist's discretion.

Please cite this article in press as: Ouchi K, Sugiyama K. Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study. Rev Bras Anestesiol. 2016. http://dx.doi.org/10.1016/j.bjane.2015.12.004

Table 1 Demographics of patients in the remifentanil use and non-use groups.

	Age (years)	Height (cm)	Weight (kg)	Male/female
Remifentanil group	43.5 ± 17.1	162.8 ± 8.9	60.4 ± 12.3	21/22
Nonuse group	41.8 ± 15.0	160.8 ± 10.4	57.7 ± 12.0	25/19
p-Value	0.61	0.35	0.32	0.52

	Anesthesia time (min)	Operation time (min)	Infusion volume (mL)	Blood loss (mL)
Remifentanil group	209.1 ± 70.5	120.8 ± 64.3	981 ± 349	19.3 ± 18.0
Nonuse group	184.5 ± 84.5	104.6 ± 76.9	862 ± 351	26.6 ± 40.5
p-Value	0.15	0.30	0.12	0.30

Anesthesia protocol

According to current recommendations, patients were allowed solid foods for up to the night before surgery, and clear fluids for up to 2.5 h before general anesthesia induction. An intravenous line was secured for administration of the isotonic fluid (140 mEq/L sodium with 1% glucose; Physio140, Otsuka Pharmaceutical, Co., Ltd., Tokyo, Japan). Furthermore, all patients continuously underwent non-invasive blood pressure and electrocardiographic monitoring using a standard automated monitoring device (Marquette Solar 8000M, GE Medical Systems, UK). Anesthesia was induced with propofol 1.5 mg/kg IV, and intubation was facilitated with the IV administration of rocuronium 0.9 mg/kg. In remifentanil-use cases, it was administered at the rate of 0.25 μg/kg/min during anesthesia induction. Anesthesia was maintained with sevoflurane (1.5%), nitrous oxide (4 L/min) and oxygen (2 L/min). Remifentanil-use cases additionally received a continuous infusion of remifentanil at the rate of 0.05–0.15 μg/kg/min. Remifentanil non-use patients did not receive any opioids. Remifentanil-use patients did not receive other opioids. Local anesthesia was used by the surgeons, as appropriate. The surgeons were unaware of the use or non-use of remifentanil. Rocuronium was administered for intubation, with no additional doses being administered intraoperatively. All patients received 4.5 mL/kg/h of the crystalloid fluid with an infusion pump from the time of securing the intravenous line. Urethral catheterization was performed after anesthesia induction and urine output was measured every 30 min during anesthesia. If patients developed hypotension intraoperatively, with a fall in systolic BP to less than 80 mm/Hg, remifentanil infusion was temporarily discontinued, and they were given ephedrine. These patients were then excluded from the study. All anesthetics were stopped at the end of surgery.

Measurement of parameters

We measured the total volume of urine (mL) and volume of urine per kilogram body weight per unit time (mL/kg/h) in all patients. We then compared these values between remifentanil use and non-use groups.

Statistical analyses

Continuous demographic and laboratory variables were compared using the unpaired *t*-test, and the Chi-square test was used for categorical variables. JMP software (version 10, SAS Institute Inc., Japan) was used for statistical analysis, and $p < 0.05$ was regarded as being statistically significant. The results are presented as mean ± SD.

Results

Eighty-seven patients were included in this study and were categorized into the remifentanil group ($n = 43$) or remifentanil non-use group ($n = 44$). Table 1 shows the patients' demographic data and Table 2 lists the surgical procedures performed. Use of remifentanil was at the attending anesthesiologist's discretion. The study subjects were attended to by one of the four anesthesiologists. Anesthesiologists A and B routinely administer remifentanil, and anesthesiologists C and D do not routinely administer remifentanil. In cases in which it was used, remifentanil was given in the dose range of 0.05–0.15 μg/kg/min. Blood pressure during the intraoperative period decreased by more than 15–25% compared with pre-anesthesia values in both groups.

Volume of urine (mL) and volume of urine per kilogram body weight per unit time (mL/kg/h) were not significantly different between the two groups (remifentanil group, 372.3 ± 273.5 mL, 1.8 ± 1.1 mL/kg/h; non-use group, 343.3 ± 283.3 mL, 1.9 ± 1.2 mL/kg/h; $p = 0.63$; 0.57, respectively) (Table 3).

Table 2 Surgeries performed in the study subjects.

	Remifentanil group	Nonuse group
Tooth extraction	15	19
Cyst extirpation	15	16
Plates exclusion	4	2
Dental treatment	2	2
Cleft lip nasal deformity	1	2
Dental implant	1	0
Incisional drainage	1	0
Sialolith extirpation	1	0
Bone transplantation	0	1
Osteoplasty	2	1
Leukoplakia excision	1	1
Number of total cases	43	44

Please cite this article in press as: Ouchi K, Sugiyama K. Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study. Rev Bras Anestesiol. 2016. http://dx.doi.org/10.1016/j.bjane.2015.12.004

Table 3 Urine output with and without the use of remifentanil during dental/minor oral surgery.

	Urine output (mL)	Weightily hourly urine output (mL/kg/h)
Remifentanil group	372.3 ± 273.5	1.8 ± 1.1
Nonuse group	343.3 ± 283.3	1.9 ± 1.2
p-Value	0.63	0.57

Discussion

The purpose of this study was to evaluate the effect of remifentanil on urine output in patients undergoing minor oral and maxillofacial surgery under general anesthesia with nitrous oxide and sevoflurane. The authors hypothesized that remifentanil would increase urine output during oral surgeries, similar to that during laparoscopic surgeries, as well as cardiac and gynecological procedures. We found, however, that remifentanil does not increase urine output during dental and oral surgery. The mechanism of the previously reported increase in urine volume by remifentanil is believed to be as follows. Adequate analgesia with remifentanil reduces the secretion of antidiuretic hormone, resulting in an increase in urine output. One of the previous reports states that the increase in urine volume induced by remifentanil is accompanied by a decrease in catecholamine secretion and a highly significant decrease in cortisol excretion.[1] In other reports, although the levels of antidiuretic hormone, catecholamine and cortisol were not measured, their values were believed to have decreased.[1,3–5] In all of these previous reports, the surgeries performed were those in which local anesthesia alone would not provide adequate analgesia. In laparoscopic surgery for example, because a wide range of analgesia is required for incision of the peritoneum, epidural anesthesia does not provide adequate analgesia.[1] Moreover, in laparoscopic surgery, a comparatively higher dose of remifentanil is required to decrease the catecholamine secretion induced by surgical stimulation.[6] Remifentanil influences the release of stress response markers, such as antidiuretic hormone, ACTH, cortisol, noradrenaline and adrenaline.[7,8] In this study, in both the groups, irrespective of the use or non-use of remifentanil, anesthesia was maintained with sevoflurane 1.5%, nitrous oxide 66.6% and oxygen 33.3%. Consequently, patients received 1.51 MAC of inhalational anesthetics, because 1 MAC of sevoflurane is 1.71% and that of nitrous oxide is 105%. Thus, the concentration of anesthetics was sufficient for minor surgery. The procedures evaluated in this study included minor oral surgeries, such as tooth extraction and cyst extirpation. Minor oral surgery is usually performed under local anesthesia or local anesthesia and intravenous anesthesia/sedation (non-use of opioids). Even cleft lip deformity can be repaired under local anesthesia.[9] Thus, in operations in this study, local anesthesia and inhalation anesthetics provided adequate analgesia in all subjects, even those who did not receive remifentanil. We postulate that the absence of an increase in urine output under remifentanil analgesia during minor oral and dental surgery, as seen in this study, is due to the fact that in these procedures, anesthesia without remifentanil provides enough analgesia that the stress response, and hence, stress hormones release is blunted, which results in minimal effect of remifentanil on these hormones and hence, on urine output.

There has been no study investigating the direct effect of remifentanil on renal function. However, previous studies on the preconditioning effect of remifentanil have reported that although remifentanil is a μ-receptor agonist, its cardioprotective effect is mediated through κ and δ opioid receptors. Reportedly, κ receptor action may increase urine output, because κ agonists have been reported to induce diuresis in animal studies.[10,11] However, urine output was not greater in the remifentanil group in this study. This suggests that κ receptor action is not responsible for the increase in urine output induced by remifentanil. Further studies are needed to elucidate the mechanism of the diuresis induced by remifentanil.

The type of fluid administered intraoperatively may affect urine output. It is reported that during use of 0.9% saline, increased afferent arteriolar resistance reduces renal flow and glomerular filtration rate, leading to reduced urine output.[12] Consequently, different types of fluids may have different effects on urine output. Thus, fluid infusion in this study was restricted to a single type of fluid. In this study, fluid was infused at the rate of 4.5 mL/kg/h. For a 60 kg patient, which was the mean weight of subjects in this study, this amounted to 270 mL/h. If fluid requirement is calculated based on the 4-2-1 rule (4 mL/kg/h for the first 10 kg body weight, 2 mL/kg/h from 11 to 20 kg and 1 mL/kg/h for every kg above 20 kg), this would have amounted to 100 mL/h for a 60 kg patient. Thus, the amount of maintenance fluid administered during anesthesia was an over dose, although the reason for this over-infusion was to compensate for preoperative dehydration over the short time period of the operation (planned for 0.5–2 h).

In this study, use of remifentanil was at the attending anesthesiologist's discretion. While the decision to use or not use remifentanil differs according to the anesthesiologist, the number of patients in the two groups in this study was almost identical. Further, since the rest of the anesthesia protocol, other than use or non-use of remifentanil, was prescribed, the likelihood of operator bias, in terms of the attending anesthesiologist, in this study is minimal.

Not all minor oral surgical procedures are performed under general anesthesia. However, even if the surgery can be adequately performed under local anesthesia or local anesthesia and intravenous anesthesia/sedation, in a previous study, patients who underwent surgery under general anesthesia reported a higher satisfaction rate with the procedure as compared to patients who had surgery under intravenous sedation.[13] Thus, general anesthesia improves patient satisfaction. Hence, although anesthesia for minor oral surgery and dental treatment does not necessarily need remifentanil, if given, it provides adequate analgesia against the stimulus of laryngoscopy and intubation. Hence, even during anesthesia for minor oral surgery and dental treatment, use of remifentanil is clearly not inappropriate.

Please cite this article in press as: Ouchi K, Sugiyama K. Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study. Rev Bras Anestesiol. 2016. http://dx.doi.org/10.1016/j.bjane.2015.12.004

Conclusions

In conclusion, our results suggest that use of remifentanil does not increase urine output during general anesthesia with nitrous oxide and sevoflurane for dental and minor oral surgery.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

This work was supported by the Departmental Research Fund of Kagoshima University. This work was presented, in part, on October 10–12, 2014, at the 42th Annual Meeting of the Japanese Dental Society of Anesthesiology (Chairperson: Prof. Kimito Sano), Niigata.

References

1. Ishikawa K, Sakai A, Nagata H, et al. Remifentanil increases urine output in patients undergoing laparoscopic colectomy. Masui. 2012;61:526–30.
2. Myles PS, Hunt JO, Fletcher H, et al. Remifentanil, fentanyl, and cardiac surgery: a double-blinded, randomized, controlled trial of costs and outcomes. Anesth Analg. 2002;95:805–12 [table of contents].
3. Onaka M, Yamamoto H. Remifentanil may be beneficial to urinary output under epidural-based general anesthesia. Masui. 2010;59:1391–5.
4. Yago Y, Tajiri O, Ito H, et al. Effect of remifentanil on urine output during gynecological laparoscopic surgery. Masui. 2009;58:613–5.
5. Kawai M, Nakata J, Kawaguchi M, et al. Comparison of urinary output during general anesthesia, between patients administered with remifentanil and those without remifentanil administration. Masui. 2010;59:179–82.
6. Myre K, Raeder J, Rostrup M, et al. Catecholamine release during laparoscopic fundoplication with high and low doses of remifentanil. Acta Anaesthesiol Scand. 2003;47:267–73.
7. Marana E, Scambia G, Colicci S, et al. Leptin and perioperative neuroendocrine stress response with two different anaesthetic techniques. Acta Anaesthesiol Scand. 2008;52:541–6.
8. Winterhalter M, Brandl K, Rahe-Meyer N, et al. Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanil infusion to intermittent fentanyl. Eur J Anaesthesiol. 2008;25:326–35.
9. Lalonde DH, Price C, Wong AL, et al. Minimally painful local anesthetic injection for cleft lip/nasal repair in grown patients. Plast Reconstr Surg Glob Open. 2014;2:e171.
10. Kim JE, Lee JS, Kim MK, et al. Nicardipine infusion for hypotensive anesthesia during orthognathic surgery has protective effect on renal function. J Oral Maxillofac Surg. 2014;72:41–6.
11. Ashton N, Balment RJ, Blackburn TP. Kappa-opioid-induced changes in renal water and electrolyte management and endocrine secretion. Br J Pharmacol. 1989;97:769–76.
12. Santi M, Lava SA, Camozzi P, et al. The great fluid debate: saline or so-called ''balanced'' salt solutions? Ital J Pediatr. 2015;41:47.
13. Mehra P, Arya V. Temporomandibular joint arthrocentesis: outcomes under intravenous sedation versus general anesthesia. J Oral Maxillofac Surg. 2015;73:834–42.

Please cite this article in press as: Ouchi K, Sugiyama K. Remifentanil does not increase urine output during oral surgery, contrary to its effect during other surgeries – a cohort study. Rev Bras Anestesiol. 2016. http://dx.doi.org/10.1016/j.bjane.2015.12.004